PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/HU2004/000123	International filing date *(day/month/year)* 18.12.2004
Priority date *(day/month/year)* 19.12.2003	
International Patent Classification (IPC) or both national classification and IPC INV. A61K31/135 A61K31/343 A61K31/381 A61K31/4525 A61K31/485 A61K31/53 A61K31/55 A61K31/675	
Applicant RICHTER GEDEON VEGYESZETI GYAR RT.	

1. This opinion contains indications relating to the following items:

   - ☒ Box No. I Basis of the opinion
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

   If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

   If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

   For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Trifilieff-Riolo, S Telephone No. +49 89 2399-7514

Form (PCT/ISA/237) (Cover Sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/HU2004/000123

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/HU2004/000123

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 16-23 (IA)

because:

☒ the said international application, or the said claims Nos. - relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/HU2004/000123

Box No. V Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3-8,11-15,17,19-23
	No:	Claims	1,2,9,10,16,18
Inventive step (IS)	Yes:	Claims	4-7,12-15,20-23
	No:	Claims	1-3,8-11,16-19
Industrial applicability (IA)	Yes:	Claims	1-15, 16-23 (see sep. sheet)
	No:	Claims	

2. Citations and explanations

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.
PCT/HU2004/000123

Re Item III.

1. Claims 16-23 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V.

Reference is made to the following documents:
D1: Epilepsia, 33(3), 1992
D2: Pharmacological res., 39(6), 1999
D3: J. Clin. Psy., 57 (s. 1), 1996

1. D1 describes pharmaceutical compositions comprising fluoxetine and ameltolide, fluoxetine and phenytoin, fluoxetine and carbamazepine (p. 574, left-hand column) and shows that fluoxetine (a ssri) enhances the anticonvulsant effects of the other compounds (known in the art as being Na channel blockers).
The subject-matter of claims 1, 2, 9, 10, 16 and 18 is not novel (A. 33(2)).

2. According to D2 sertraline does not exert any influence on carbamazepine used as anticonvulsant.
The teaching of D3 is similar and concerns the absence of effect of fluoxetine when used together with the anticonvulsant phenytoin.
These documents, as well as D1, are cited in the present description which summarizes the teaching of the prior art as being controversial (p. 3, l. 25-28).

The present invention concerns a combination of "a sodium channel blocker" and "a selective serotonin uptake inhibitor" which is to be used to treat various diseases, such as "alcohol addiction, incontinence, inflammation, epilepsy etc...".
The following effects are shown by the present application:
enhanced anti-tremor activity of lamotrigine when used in combination with fluoxetine (p. 10)

enhanced anti-convulsant activity of lamotrigine and crobenetine when used in combination with fluoxetine or sertraline (p. 10, Table 2)
slightly better side effects profile when lamotrigine and crobenetine are used in combination with fluoxetine or sertraline (p. 11, Table 3)
enhanced analgesic activity of lamotrigine when used in combination with fluoxetine (Fig. 5).

In view of the fact that some pieces of prior art do not show any synergistic anticonvulsant effect due to sertraline or fluoxetine (D2, D3), it cannot be accepted that any sodium channel blocker combined with any selective serotonin uptake inhibitor will lead to a synergistic anticonvulsant effect.
Thus the problem consisting in providing a composition comprising a known anticonvulsant possessing an enhanced anticonvulsant effect with respect to the known anticonvulsant alone is not solved over the whole scope of claims 3, 11 and 19.

Similarly as the application contains no data concerning the treatment of the diseases enumerated in claims 8 and 17, it cannot be assessed whether the problem of providing a remedy to these (very different) diseases is solved.

Therefore no inventive step can be acknowledged for the subject-matter of claims 3, 8, 11, 17 and 19 (A. 33(3)).

3. For the assessment of the present claims 16-23 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.